

Adherence to lipid-lowering medications and cardiovascular disease prevention in type 2 diabetes mellitus

Akademisk avhandling

Som för avläggande av farmacie doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i rum 2118, Arvid Wallgrens Backe, hus 2 den 30 november 2018, klockan 9.00

av Sofia Axia Karlsson

Fakultetsopponent:
Professor Petra Denig
University of Groningen, Nederländerna

Avhandlingen baseras på följande delarbeten

- I. Karlsson SA, Hero C, Eliasson B, Franzén S, Svensson AM, Miftaraj M, Gudbjörnsdóttir S, Eeg-Olofsson K, Andersson Sundell K. *Refill adherence and persistence to lipid-lowering medicines in patients with type 2 diabetes: A nationwide register-based study*. *Pharmacoepidemiology and Drug Safety* 2017; 26(10): 1220-1232.
- II. Karlsson SA, Hero C, Svensson AM, Franzén S, Miftaraj M, Gudbjörnsdóttir S, Eeg-Olofsson K, Eliasson B, Andersson Sundell K. *Association between refill adherence to lipid-lowering medications and the risk of cardiovascular disease and mortality in Swedish patients with type 2 diabetes mellitus: a nationwide cohort study*. *BMJ Open* 2018; 8(3): e020309
- III. Karlsson SA, Franzén S, Svensson AM, Miftaraj M, Eliasson B, Andersson Sundell K. *Prescription of lipid-lowering medications for patients with type 2 diabetes mellitus and risk-associated LDL cholesterol: a nationwide study of guideline adherence from the Swedish National Diabetes Register*. Submitted.
- IV. Karlsson SA, Eliasson B, Franzén S, Miftaraj M, Svensson AM, Andersson Sundell K. *Associations between patients' and healthcare providers' adherence to lipid-lowering medications and risk of cardiovascular events and mortality in patients with type 2 diabetes mellitus in Sweden*. Manuscript.

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Abstract

Background and aims: Globally, cardiovascular disease (CVD) is the major cause of death among patients with type 2 diabetes mellitus (T2DM). Improved control of LDL cholesterol with lipid-lowering medications and patients' adherence to such medications have been shown associate with lower risk of CV events and mortality among T2DM patients. The impact of healthcare providers' adherence to guidelines regarding prescription for lipid-lowering medications is unclear. This thesis aimed to assess and compare i) patients' adherence to lipid-lowering medications, ii) healthcare providers' adherence to lipid-lowering prescription guidelines, and iii) risk of CV events and mortality in relation to patients' adherence to lipid-lowering medication and healthcare providers' guideline adherence among patients with T2DM.

Patients and methods: This thesis is based on four observational studies where individualized data were linked between Swedish National Registers. All studies included data about patients with T2DM of at least 18 years of age. To assess patients' adherence, our studies used information about new users of lipid-lowering medications from pharmacy claims data in the Swedish Prescribed Drug Register. Using data from the Swedish National Diabetes Register, guideline adherence was assessed for healthcare providers who treated patients with T2DM and LDL cholesterol above the recommended target values. We used information about cause of death and completed admissions of in and out-patients care to analyze risk of CV events and mortality, adjusted for sex, age, socioeconomic status, and concurrent medications as well as health-related and clinical characteristics.

Results: On average, patients' adherence to lipid-lowering medications was higher among secondary prevention patients, smokers and those with concurrent cardioprotective medications, compared to lower adherence among patients born outside of Sweden. Healthcare providers' adherence to lipid-lowering prescription guidelines was higher among patients attributed to secondary prevention and the odds of receiving a prescription associated with patients' individual risk of CV events. Adjusted for potential confounders, risk of CV events was higher among patients with less than complete adherence to lipid-lowering medications and that risk gradually increased as patient adherence declined, independent of prevention group. Healthcare providers' adherence to guidelines had little or no impact on patients' risk of CV events and mortality.

Conclusions: Patients' adherence to lipid-lowering medications among patients with T2DM had greater impact on risk of CV events and mortality compared to healthcare providers' adherence to prescription guidelines for such medications. This thesis emphasizes the value of individualized diabetes care among T2DM patients.

Keywords: medication adherence, refill adherence, medication persistence, pharmacoepidemiology, lipid-lowering medications, type 2 diabetes mellitus, cardiovascular disease, all-cause mortality, cardiovascular mortality, guideline adherence